Claims

1. A method of producing dopaminergic neuronal cells suitable for transplantation in dopamine deficiencies, said transplantable neuronal cells being derived from progenitor cells,

a. providing progenitor cells which lack at least one indicator of neuronal cell differentiation;

b. treating the progenitor cells with an inducing agent for a time period sufficient to optimize expression of tyrosine hydroxylase and to induce the presence of at least one indicator of neuronal cell differentiation to produce a plurality of dopaminergic, differentiated neuronal cells; and

c. minimally replating with an inhibitor to optimize the dopaminergic phenotype and a purified harvest; and.

d. harvesting the dopaminergic, differentiated neuronal cells.

2. The method of claim 1, wherein the step of providing progenitor cells provides mammalian cells.

3. The method of claim 1, wherein the step of providing progenitor cells provides human NT2/D1 cells.

4. The method of claim 1, wherein the step of providing progenitor cells provides mammalian fetal cells.

5. The method of claim 1, wherein the step of providing progenitor cells provides mammalian stem cells.

6. The method of claim 1, wherein step (c) also includes adding at least one lithium salt.

7. The method of claim 1, wherein step (c) is followed by an additional step of co-culturing with at least one cell type which stabilizes or improves the dopaminergic phenotype of the cells.

8. The method of claim 7, wherein the co-culturing step is co-culturing with human bone

marrow stem cells, fetal stem cells, or Sertoli cells.

9. The method of claim 7 wherein the co-culturing step comprises co-culturing with Sertoli cells, human bone marrow stem cells, or a combination thereof.

10. The method of claim 1 wherein the step of treating the progenitor cells comprises applying retinoic acid or retinoids thereto.

11. A dopaminergic neuronal cell suitable for transplantation into an individual having a dopaminergic deficiency, said cell comprising

a post-mitotic differentiated neuronal cell which expresses tyrosine hydroxylase and at least one other indicator of neuronal cell differentiation, said cell having undergone induction from an undifferentiated cell.

12. A human post-mitotic dopaminergic cell suitable for transplantation into a human having a dopaminergic deficiency, said cell comprising a differentiated neuronal cell which expresses tyrosine hydroxylase and at least one other indicator of neuronal cell differentiation, said cell having undergone induction from an undifferentiated human cell.

13. A human dopaminergic cell suitable for transplantation into a human having a dopaminergic deficiency, the cell comprising a differentiated human neuronal cell that expresses tyrosine hydroxylase and bcl-2, said cell being capable of synthesizing dopamine and having improved survival after transplantation.

14. A method of improving the survival of human neuronal cells for transplantation, said method comprising the steps of

a. providing a culture of human cells;

b. adding a lithium salt to the human cell culture for a sufficient time to enhance expression of bcl-2;

c. testing cells from the treated cell culture for the presence of bcl-2; and

d. isolating the cells from the culture to produce an isolated cell preparation; and

e. testing the isolated cell preparation for sterility before packaging the cells for transport.

15. A pharmaceutical dosage form of human non-fetal cells suitable for transplantation in Parkinson's Disease comprising

isolated, purified, neuronal cells, the neuronal cells expressing tyrosine hydroxylase, D2 dopamine receptor, and aldehyde dehydrogenase-2; and

a pharmaceutical diluent.

16. The transplantable neuronal cells of claim 13, wherein the lithium salt is lithium chloride.

17. The method of claim 15, wherein the lithium salt is lithium chloride.

18. A chimeric non-human mammal wherein the mammal comprises post-mitotic dopaminergic neuronal cells implanted in the brain of the mammal.

19. A method of preparing human neuronal cells suitable for treating Parkinson's Disease, the method comprising:

a) providing NT2/D1 cells;

b) culturing NT2/D1 cells with an inducing agent for a time sufficient to optimize TH expression therein;

c) replating and culturing the TH-optimized cells in mitotic inhibitor; and

d) separating the TH-optimized neuronal cells from the replate culture.

20. The method of claim 19, additionally comprising the steps of

e) replating the TH-optimized cells on a confluent feeder cell layer, the cell layer being chosen from cells which stabilized TH production, including bone marrow stem cells, TM4 Sertoli cells, glioma cells, or a combination thereof; and

f) isolating the TH-optimized and stabilized cells from the replate medium.

21. A pharmaceutical composition for treating Parkinson's Disease , the composition comprising

isolated, purified, neuronal cells, the neuronal cells expressing tyrosine hydroxylase, D2 dopamine receptor, and aldehyde dehydrogenase-2;

cells capable of stabilizing tyrosine hydroxylase production; and

a pharmaceutical diluent.

22. The composition of claim 21 in which the stabilizing cells are Sertoli cells, bone marrow stem cells or a combination thereof.

23. A purified human dopaminergic cell type, the cells having been cultured from NT2 cells, treated for about two to three weeks with an inducing agent, cultured for about two weeks with growth media without an inducing agent or mitotic inhibitor, cultured for about one week with at least one mitotic inhibitor, harvested and placed in a diluent.

24. A method of producing neurotransmitter phenotype cells, selected from the group of dopaminergic, serintinergic, cholinergic, and gabanergic cells, suitable for transplantation in neurodegenerative deficiencies or abnormal neurological conditions, said transplantable neurotransmitter phenotype cells being derived from progenitor cells,

a. providing progenitor cells which lack at least one indicator of neuronal cell differentiation;

b. treating the progenitor cells with an inducing agent for a time period sufficient to optimize expression of a specific neurotransmitter marker and to induce the presence of at least one indicator of neuronal cell differentiation to produce a plurality of desired neuronal cells; and

c. minimally replating with an inhibitor to optimize the desired phenotype and a purified harvest; and.

d. harvesting the desired neuronal cells.

25. A neurotransmitter phenotype cell selected from the group of dopaminergic, serintinergic, cholinergic, and gabanergic cells, suitable for transplantation into an individual having a neurodegenerative deficiency, said cell comprising

a post-mitotic differentiated neuronal cell which expresses a specific neurotransmitter marker and at least one other indicator of neuronal cell differentiation, said cells having undergone induction from an undifferentiated cell.

26. A human post-mitotic neurotransmitter cell suitable for transplantation into a human

having a neurodegenerative deficiency, said cell comprising a differentiated neuronal cell which expresses a specific neurotransmitter marker and at least one other indicator of neuronal cell differentiation, said cell having undergone induction from an undifferentiated human cell.

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27. A chimeric non-human mammal wherein the mammal comprises post-mitotic neurotransmitter phenotype neuronal cells, selected from the group of dopaminergic, serintinergic, cholinergic, and gabanergic cells, implanted in the brain of the mammal.